

Docket No.: 13111-00020-US  
(PATENT)

En 1626

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:  
Stürmer et al.

Confirmation No.: 2164

Application No.: 10/522888

Group Art Unit: 1626

Filed: February 1, 2005

Examiner: Not Yet Assigned

For: METHOD FOR THE PRODUCTION OF (S)-3-METHYLAMINO-1-(THIEN-2-YL) PROPAN-1-OL

**TRANSMITTAL OF TRANSLATION OF INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Applicants enclose herewith the Translation of the International Preliminary Examination Report. The Examiner will note that the International Preliminary Examining Authority deemed that claims 1-9 were novel, had inventive step and industrial applicability.

Applicants believe no fee is due with this communication. However, if a fee is due, the Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 03-2775, under Order No. 13111-00020-US, from which the undersigned is authorized to draw.

Respectfully submitted,

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PTO/SB/92 (09-04)

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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application No.: 10/522888

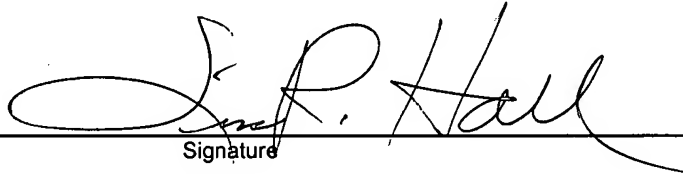
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## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference M/43022	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP2003/008492	International filing date (day/month/year) 31 July 2003 (31.07.2003)	Priority date (day/month/year) 01 August 2002 (01.08.2002)
International Patent Classification (IPC) or national classification and IPC C07D 333/20, C07B 57/00		
Applicant BASF AKTIENGESELLSCHAFT		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of \_\_\_\_\_ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 07 January 2004 (07.01.2004)	Date of completion of this report 13 December 2004 (13.12.2004)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP2003/008492

## I. Basis of the report

## 1. With regard to the elements of the international application:\*

- ☒ the international application as originally filed
- ☒ the description:  
pages 1-20, as originally filed  
pages \_\_\_\_\_, filed with the demand  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☒ the claims:  
pages 1-9, as originally filed  
pages \_\_\_\_\_, as amended (together with any statement under Article 19  
pages \_\_\_\_\_, filed with the demand  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the drawings:  
pages \_\_\_\_\_, as originally filed  
pages \_\_\_\_\_, filed with the demand  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the sequence listing part of the description:  
pages \_\_\_\_\_, as originally filed  
pages \_\_\_\_\_, filed with the demand  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

## 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

## 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/fig \_\_\_\_\_

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

## 1. Statement

Novelty (N)	Claims	1-9	YES
	Claims		NO
Inventive step (IS)	Claims	1-9	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-9	YES
	Claims		NO

## 2. Citations and explanations

The assessment of the present application was based on the following search report documents:

D1: PAMIES, O.; BÄCKVALL, J. E.: 'Efficient Lipase-Catalyzed Kinetic Resolution and Dynamic Kinetic Resolution of beta-Hydroxy Nitriles. A Route to Useful Precursors for gamma-Amino Alcohols' ADVANCED SYNTHESIS AND CATALYSIS, Vol. 343, No. 6-7, 2001, pages 726-731

D2: DEETER J ET AL: 'ASYMMETRIC SYNTHESIS AND ABSOLUTE STEREOCHEMISTRY OF LY248686' TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, Vol. 31, No. 49, 26 November 1990 (1990-11-26), pages 7101-7104

D3: US-A-5 491 243 (BERGLUND RICHARD A)  
13 February 1996

D4: EP-A-0 650 965 (LILLY CO ELI) 3 May 1995

D5: EP-A-0 457 559 (LILLY CO ELI) 21 November 1991

D6: EP-A-0 273 658 (LILLY CO ELI) 6 July 1988.

(1) The present application deals with a method for the enantiomerically pure preparation of an intermediate product II-S; this compound is then to be used for the preparation of the antidepressant duloxetine.

The claimed method essentially comprises the reaction of a mixture of two alcohols I-S and I-R with an acylating agent

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/08492
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in the presence of a hydrolase. The desired alcohol II-S is obtained subsequently.

The prior art documents D2 to D6 deal with other types of methods for the enantiomerically pure preparation of the target molecules (for example, racemate separation or use of optically active salts).

(2) Document D1 is considered to be the closest prior art. D1 already discloses the claimed method (cf. tables 1 and, in particular, 3), but using different types of radicals in position 3 of the propionitrile. Novelty is therefore acknowledged (PCT Article 33(2)).

(3) In document D1, according to table 3, different groups R have been used, including, for example, 2-furyl, 3-pyridyl or phenyl. A person skilled in the art would therefore have been capable of replacing these radicals by a 2-thiophenyl group. On the other hand, on the basis of the applicant's explanations, it is granted that in D1 the S-enantiomer is obtained in acylated form, whereas in the claimed method non-acylated S-alcohol is obtained as well as acylated R-alcohol. This must be rated as a surprising finding on the basis of D1 and the presence of an inventive step (also taking into consideration the ee values on page 19 of the description) is acknowledged (PCT Article 33(3)).